A Survey of Pediatric Critical Care Providers on the Presence, Severity, and Assessment of Capillary Leak in Critically Ill Children

Richard Pierce¹ Peter M. Lockett² Edward Vincent S. Faustino¹

¹Department of Pediatrics, Yale School of Medicine, New Haven, Connecticut, United States

²Department of Pediatrics, University of Texas Southwestern Medical Center, Dallas, Texas, United States

Address for correspondence Richard Pierce, MD, Department of Pediatrics, Yale School of Medicine, 333 Cedar Street, New Haven, CT 06520, United States (e-mail: Richard.pierce@yale.edu).

J Pediatr Intensive Care 2017;6:145–151.

Abstract

Purpose To determine provider opinions on factors most commonly used to assess the presence and severity of pathologic capillary leak in critically ill children.

Methods We conducted an electronic survey of pediatric critical care providers. Patient scenarios were presented to assess opinions on the risk, presence, and clinical significance of capillary leak. Responses were obtained using Likert scales and multiple-choice questions.

Results A total of 160 responses were analyzed. Respondents agreed that capillary leak is present in the scenario with septic shock while respondents somewhat agreed that it is also present with poly-trauma, cardiac arrest, or cardiopulmonary bypass. They agreed that physical exam, but neither agreed nor disagreed that laboratory tests, can be used to assess and follow the severity of capillary leak in these children. Generalized edema, increase in weight, and pulmonary crackles were commonly identified parameters for assessing capillary leak. The patient factor most commonly identified with capillary leak was presence of infection, while treatment factors most commonly identified were cardiopulmonary bypass and general anesthesia.

Conclusion There is agreement that capillary leak is common in critically ill children and exacerbates disease. The parameters identified in this study may facilitate a more standardized clinical evaluation of pathologic capillary leak for future studies.

Keywords

- capillary leak
- endothelial cell
- pediatrics
- pediatric critical care
- survey
- vascular permeability

Introduction

In normal conditions (homeostasis), the vascular endothelium actively maintains normal permeability and appropriate intravascular volume, regulates blood flow and fluidity, and modulates inflammation and interaction with leukocytes.¹ Given these essential functions, the endothelium has been labeled the organ of the intensivist.² In the setting of critical illness, the endothelial cells of the vasculature may be “activated” to restore homeostasis or “dysfunctional” and propagate the pathophysiologic process.³ When endothelial cell dysfunction affects vessel

permeability, intravascular fluid is inappropriately distributed into the extra-vascular space. This phenomenon is referred to as “leak” (or “third spacing”) and is thought to contribute to morbidity and mortality.⁴ Most clinicians believe they “know it when they see it,” but may be unable to grade its severity in a standardized manner. The lack of consistent criteria to diagnose leak and stratify its severity impairs development of appropriate treatment regimens and hinders research in this field.

There has been great progress in understanding the mechanisms of endothelial permselectivity changes in vitro and in animal models.^{5,6} In response to inflammatory stimulation (like

received

July 4, 2016

accepted after revision

August 11, 2016

published online

September 26, 2016

Copyright © 2017 by Georg Thieme
Verlag KG, Stuttgart · New York

DOI <https://doi.org/10.1055/s-0036-1593388>.
ISSN 2146-4618.

with histamine or tumor necrosis factor- α), the venules are the first vascular segment to respond with an increase in permeability.^{7,8} This response acts to restore homeostasis with physiologically appropriate recruitment of immune cells and localized expansion of the extracellular space (i.e., endothelial cell activation). After intense or prolonged inflammatory stimulation, as seen in critical illness, the capillary segment of the vasculature increases in permeability. Clinically significant pathologic leak is almost always due to changes in the permeability of the capillary segment and may result in decreased intravascular fluid, organ parenchymal edema, impaired oxygen diffusion, and, eventually, shock and organ failure (i.e., endothelial cell dysfunction).^{9,10} Due to the massive combined surface area of the capillary vascular segment, even small changes in segmental permselectivity (the ability to regulate macromolecule flux based on size and charge) result in significant clinical impact. However, these basic science advances have yet to be successfully correlated to the clinical assessment of capillary leak in critically ill children. In animal models, capillary leak may be evaluated by posthumous organ weight and histologic examination of edema, protein deposition, or leukocyte infiltration. In adults, capillary leak, or extravascular pulmonary fluid as a surrogate, is assessed rarely by invasive trans-pulmonary thermodilution measurements, pulse index continuous cardiac output monitors (also known as PiCCO), or radiolabeled albumin dispersion studies.^{11–14} These techniques are not applicable to critically ill children due to their expense, invasive nature, and lack of clinical validation. Standardized identification of capillary leak and stratification of its severity is essential to assess if the clinical course of capillary leak mirrors that observed in the frequently used animal and in vitro models.

The absence of standardized diagnostic criteria for capillary leak impairs efforts to determine its specific clinical impact and ultimately adopt comprehensive treatment strategies. We aim to identify the clinical variables most commonly associated with pathologic capillary leak in an effort to define its presence and assess its effect in critically ill children. Surveys are a useful tool in identifying relevant variables in clinical practice. Therefore, as a first step in the process of arriving at a more clear-cut definition of capillary leak, we created a survey. Our ultimate goal is to use the process described above to derive a consensus definition for pathologic capillary leak in critically ill children.

Materials and Methods

Study Design

We conducted a cross-sectional, self-administered electronic survey of pediatric critical care physicians in North America. The study was reviewed and approved by the Human Investigations Committee at Yale University School of Medicine. The survey was voluntary and anonymous, and participation implied consent.

Respondents

Target respondents of the survey were board-certified pediatric critical care physicians in North America. To generate the mailing list, hospitals with pediatric intensive

care units (PICUs) were identified from the directories of the American Hospital Association, Children's Hospital Association, American Medical Association, and Virtual PICU. Electronic mail addresses were obtained from the hospitals' Web sites and additional addresses were obtained from the membership directories of the Society of Critical Care Medicine and the Pediatric Acute Lung Injury and Sepsis Investigators (PALISI) Network. Respondents were requested to answer each survey item based on their personal opinions and experiences.

Survey Development and Administration

The survey instrument was created after literature review and pilot-tested by two content experts and revised prior to distribution. The survey was endorsed by PALISI. Items in the survey instrument were patterned after scenarios commonly associated with capillary leak: bacterial septic shock, respiratory syncytial virus (RSV) bronchiolitis, exposure to cardiopulmonary bypass, cardiac arrest, and poly-trauma. Respondents were queried regarding different parameters thought to be important in identifying the presence and severity of capillary leak. Likert scales (1 = strongly agree, 2 = agree, 3 = somewhat agree, 4 = neither agree nor disagree, 5 = somewhat disagree, 6 = disagree, 7 = strongly disagree) were used to determine agreement with specific statements regarding the presence, severity, and consequences of capillary leak in each scenario. The scenarios were followed by six multiple-choice questions with optional free-text responses. We also collected the respondents' demographics and the characteristics of their PICU.

The survey, conducted from October to December of 2015, was administered electronically using Qualtrics (Qualtrics Company, Provo, Utah, United States). Each potential respondent was sent an introduction and survey link electronically. Two reminders were sent 2 weeks apart for those who had not yet completed the survey.

Statistical Analysis

Descriptive data was presented as medians (interquartile ranges [IQR]) to account for the ordinal variables, or counts (percentages) for categorical variables. Friedman test was used to compare the Likert responses from the case scenarios and accounted for intrarespondent correlation. Statistical significance was evaluated at a 2-sided p value of 0.05. Friedman testing for differences among repeated measures revealed significant differences of responses in one or more responses to all seven questions, indicated by $p < 0.001$ in **Table 1**. All tests were performed using Stata 14.1 (StataCorp, College Station, Texas, United States).

Results

Characteristics of the Respondents

We initially sent the introduction to the survey to 797 electronic addresses; of these, 64 messages could not be delivered. A maximum of two reminders were sent to nonresponders. A total of 160 physicians participated in the survey (22% response rate) with 115 of them

Table 1 Median and interquartile range for Likert responses in all case scenarios

Question	Median response (IQR) for case scenarios					p-value
	Septic shock	Poly-trauma	Cardiac arrest	CPB	RSV	
Q1. This patient has capillary leak.	2 (3.5, 2)	3 (4, 2)	3 (4, 2)	3 (4, 2)	4 (6, 4)	< 0.001
Q2. Capillary leak is a contributing factor to this patient's critical illness.	2 (3, 1)	3 (4, 2)	4 (4, 2)	4 (4, 2)	4 (6, 4)	< 0.001
Q3. The severity of capillary leak in this patient can be assessed and followed via the physical exam.	3 (3, 2)	3 (4, 2)	3 (4, 2)	3 (4, 2)	3 (4, 3)	< 0.001
Q4. The severity of capillary leak in this patient can be assessed and followed with laboratory tests.	4 (5, 3)	4 (5, 3)	4 (5, 3)	4 (6, 3)	4 (6, 3)	< 0.001
Q5. This patient's illness will be exacerbated by the severity of capillary leak.	2 (2, 1)	2 (3, 2)	2 (3, 2)	2 (3, 2)	3 (4, 2)	< 0.001
Q6. The presence of capillary leak will change how I manage the patient.	2.5 (3, 2.5)	2 (3, 2)	2 (3, 2)	2 (3, 2)	3 (4, 2)	< 0.001
Q7. Management decisions may lead to worsening of this patient's capillary leak.	2 (3, 2)	2 (3, 2)	2.5 (3, 2)	2 (3, 2)	3 (4, 2)	< 0.001

Abbreviations: CPB, cardiopulmonary bypass; IQR, interquartile range; RSV, respiratory syncytial virus.

Note: Results of the responses from the case scenarios, listed as median (interquartile range). Friedman testing for repeated measures within groups revealed significant differences among the set of responses compared across each case scenario ($p < 0.001$, see text). The Likert scale used was 1 = strongly agree, 2 = agree, 3 = somewhat agree, 4 = neither agree nor disagree, 5 = somewhat disagree, 6 = disagree, 7 = strongly disagree.

responding to all items (72% completion rate). The responses from 160 physicians were analyzed. Respondents mostly graduated fellowship between 2000 and 2009 (30%) (►Table 2). They tended to spend >50 to 75% of their professional time in clinical practice (33%), in a mixed medical-surgical PICU (52%), in a PICU with 11 to 20 beds (42.7%), and in an academic hospital setting (97%).

Presence and Severity of Capillary Leak in Critically Ill Children

In general, respondents somewhat agreed that capillary leak was present in the child with septic shock, poly-trauma, cardiac arrest, or cardiopulmonary bypass (►Table 1). However, respondents neither agreed nor disagreed that capillary leak was present in the scenario of the child with RSV bronchiolitis. Respondents agreed that the presence of capillary leak would contribute to disease severity in the child with septic shock and somewhat agreed for the child with poly-trauma but not for the other children. Respondents somewhat agreed that the presence of capillary leak would exacerbate the severity of illness. They somewhat agreed that the severity of capillary leak can be assessed and followed via physical exam but neither agreed nor disagreed that this can be assessed and followed with laboratory tests. They agreed that the patient's illness will be exacerbated by the severity of capillary leak, its presence would change management, and management decisions could lead to worsening of capillary leak for all children except for the child with RSV. Friedman testing comparing the set of responses within a scenario to the set of responses in each other scenario revealed statistically significant differences between all scenarios.

Table 2 Characteristics of respondents

Characteristic	Responses (%), n = 115
Year of pediatric critical care fellowship completion	
2010 or more recently	29 (25%)
2000 to 2009	34 (30%)
1990 to 2000	21 (18%)
1980 to 1990	29 (25%)
1980 or earlier	2 (2%)
Description of unit	
Pediatric medical-surgical ICU	60 (52%)
Pediatric cardiac ICU	5 (4%)
Mixed pediatric medical-surgical and cardiac ICU	50 (43%)
Description of practice environment	
Academic hospital	113 (98%)
Community hospital	2 (2%)
How much clinical service time	
Less than 25%	9 (8%)
25 to 50%	37 (32%)
50 to 75%	38 (33%)
More than 75%	31 (27%)
Additional training	
None	86 (75%)
Additional non-PICU pediatric training	22 (19%)
Additional non-pediatric training	7 (6%)

Table 3 Patient and treatment factors that are associated with capillary leak

Patient factors (<i>n</i> = 115)	%	Treatment factors (<i>n</i> = 115)	%
Presence of infection ^a	83	Cardiopulmonary bypass ^a	86
Nutritional status	46	General anesthesia ^a	74
Type of infection	41	Extra-corporeal membranous oxygenation ^a	64
Genetic susceptibility to vascular leak	41	Crystalloid resuscitation ^a	54
Other (ischemia, inflammation, degree of insult)	17	Aortic cross-clamp	48
Age	8	Renal replacement therapy	17
Weight	2	Mechanical ventilation	17
Gender	0	Treatment with antibiotics	14
		Use of vasoactive medications	9
		Other (albumin administration, sedation)	9

Note: Patient and treatment factors listed with the percent (%) of responders who associated them with capillary leak.

^aDenotes parameters selected for incorporation into forthcoming structured patient scenarios.

Factors That Affect the Presence of Capillary Leak in Critically Ill Children

Respondents selected multiple factors that might increase concern for the presence of capillary leak (►Table 3). Patient factors thought to be associated with capillary leak were the presence of infection (83% of respondents), nutritional status (46%), type of infection (41%), and a genetic predisposition to capillary leak (41%). Treatment factors thought to be associated with capillary leak included cardiopulmonary bypass (86%), general anesthesia (74%), extra-corporeal membranous oxygenation (ECMO, 65%), crystalloid resuscitation (52%), and aortic cross-clamp (48%).

Factors Used to Assess the Presence and Extent of Capillary Leak in Critically Ill Children

The components of the physical exam that were thought most commonly used to determine the presence or severity of capillary leak were generalized edema (98%), increase in weight (79%), and pulmonary crackles (70%) (►Table 4). The laboratory tests most commonly included albumin (68%) and blood urea nitrogen (39%) (►Table 4).

Discussion

This self-administered electronic survey provides insight into the diverse opinions of providers on the etiology and evolution of capillary leak. Our survey indicates that pediatric critical care physicians in North America believe that capillary leak is present and clinically impactful in a wide range of disease states. Physical exam findings seemed more important than laboratory tests in assessing and following the severity of capillary leak. We have identified patient and treatment factors believed by the respondents to be associated with risk of developing capillary leak. These findings are important in deriving a definition for pathologic capillary leak in critically ill children.

Conceptually, capillary leak must arise from perturbations in the variables of Starling Hypothesis, which describes fluid flux across the vascular membrane:

$$J_v = K_f [(P_c - P_i) - \sigma(\pi_c - \pi_i)]$$

Fluid flux (J_v) is dependent on the filtration coefficient (K_f), the difference between capillary and interstitial hydrostatic pressures (P_c and P_i , respectively), the reflection coefficient (σ), and the difference between capillary and interstitial oncotic pressure (π_c and π_i , respectively). The area and permeability of the endothelium determine the filtration coefficient, which can vary greatly in pediatric critical illness. The reflection coefficient is a correction factor for the decreased permeability of very large or highly charged protein molecules. Differences in both hydrostatic and oncotic pressure gradients can be altered by critical illness and by resuscitation efforts. Any pathologic flux of fluid across the endothelial barrier must arise from either vascular dysfunction (changes in K_f , also known as high-permeability edema) or changes in hydrostatic or oncotic gradients ($P_c - P_i$ or $\pi_c - \pi_i$, respectively).

Several patient and treatment factors were identified as associated with leak by the majority of respondents. The presence and type of infection were the patient factors most believed to be associated with capillary leak, and these variables would be expected to dramatically affect the endothelial filtration coefficient (K_f). Nutritional status was identified by a minority of respondents as being associated with leak. For this survey, “nutritional status” was left open ended to encourage inclusion of multiple interpretations. Conceptually, nutritional status may directly contribute to osmotic gradients detailed in Starling Hypothesis ($\pi_c - \pi_i$, such as a malnourished child with hypoalbuminemia) or affect the endothelial cell surface or function (K_f , as with glucose or nutritional support). Practically, very little is known about the relationship between nutritional status and capillary leak. Very few studies have investigated possible detrimental effects of elevated serum glucose¹⁵ and parental nutritional support^{16,17} on in vitro vascular permeability, and no studies on the clinical effects of leak in children exist. The lack of other patient factors identified likely reflects our poor

Table 4 Parameters most commonly used to assess the presence and severity of capillary leak in critically ill children

Physical exam finding	%	Other testing finding	%
Generalized edema ^a	98	Cumulative fluid balance ^a	86
Increase in weight ^a	79	Serum albumin ^a	68
Pulmonary crackles ^a	70	Urine output ^a	63
Decrease in urine output ^a	67	Chest X-ray ^a	61
Increasing oxygen requirement ^a	54	Central venous pressure monitoring ^a	59
Increasing ventilator settings	46	Blood urea nitrogen	39
Low blood pressure	37	Sodium	28
Tachycardia	33	Creatinine	23
Hepato-splenomegaly	30	Cardiac echocardiogram	21
Widened pulse pressure	30	Hematocrit	20
Cardiac gallop	16	Lactate	18
		Total serum protein	15
		Serum osmolarity	11
		Ultrasound of body edema	9

Note: Physical exam parameters and ancillary testing listed with the percent (%) of responders who associated them with capillary leak.

^aDenotes parameters selected for incorporation into forthcoming structured patient scenarios.

understanding of this phenomenon. Intensivists commonly lament that one patient may develop severe leak that complicates their care while a similar patient, with similar disease severity, may develop minimal leak. Although patient genotype was only identified by 41% of respondents as associated with leak, there are almost certainly underlying genetic factors that impact both the risk and consequences of capillary leak. However, no specific polymorphisms have been identified. A catchall response of “Other” was identified by only 17% of respondents as associated with leak, indicating etiologic uncertainty among the pediatric critical care community. There may be a selection bias, due to the limited number of possible responses, but even in review with our content experts we could not identify any additional appropriate possible responses and very few responses were written in using the available free-text response. More treatment factors (4) than patient factors (1) were identified by a majority of respondents as associated with capillary leak. General anesthesia, cardiopulmonary bypass, and ECMO are treatment factors identified that are generally thought to involve both fluid overload and a systemic inflammatory response. Altogether, these responses highlight the great uncertainty surrounding leak and the need for a concise definition of capillary leak to facilitate standardized investigations into patient and treatment risk factors.

The factors used in the assessment of capillary leak in critically ill children also displayed great variability. Although physical exam was most associated with assessment across all scenarios (►Table 1), an equal number of physical exam findings (5) and nonphysical exam findings (5) was identified by the majority of respondents. Edema, increase in weight, pulmonary crackles, positive fluid balance, and high CVP may result from fluid overload or capillary leak. Additionally, many of the factors identified in our survey do not intuitively relate to the variables in Starling Hypothesis. Taken together,

these results highlight the clinical and diagnostic uncertainty of this complex but common phenomenon.

Establishing a definition for any condition in the absence of a “gold standard” presents a significant challenge. Fortunately, methodology to address this problem has been previously established, notably for the derivation of the diagnostic criteria for systemic lupus erythematosus (SLE).^{18,19} The SLE criteria demonstrate the stepwise establishment of diagnostic criteria from expert opinion (see ►Fig. 1). Our survey is the first step of this process. We identified in this survey the parameters most commonly used to assess the presence and extent of capillary leak in critically ill children. To construct the standardized patient scenarios required for step 2, essential variables must be selected for inclusion. Given the diversity of provider opinion and the spectrum of disease severity associated with capillary leak, it is not unreasonable to include all variables identified by at least 50% of respondents. These variables include the use of cardiopulmonary bypass/ECMO/general anesthesia, crystalloid resuscitation, presence of infection, presence of peripheral edema, changes in weight, changes in urine output, cumulative fluid balance, change in oxygen saturation, serum albumin level, and chest X-ray findings.

This study has limitations. Despite two reminders, our response rate was 22.0%, not accounting for messages that were electronically filtered. Low response rates are a risk of survey research; however, we have higher response rate²⁰ and total number of responses²¹ than recently published surveys. We collected the opinions of almost a quarter of the practicing pediatric intensivists across North America. Our demographics generally match those from the Pediatric Critical Care Workforce Survey, although a higher percentage of responders are from academic centers.²² Lastly, we only surveyed pediatric critical care practitioners because they are most likely to decide on changes in therapy in response to the

Fig. 1 Steps for derivation of a consensus definition for capillary leak. This process mirrors the process used to define systemic lupus erythematosus.

presence or severity of capillary leak. Other members of the multidisciplinary care team may have different opinions on capillary leak. A survey will not adequately capture the complex interplay of these multiple factors and attitudes. However, one of the goals of a survey is to lay the foundation for future work.

Conclusion

Our survey showed that capillary leak is perceived to be a problem in critically ill children. We identified the patient risk factors, medical interventions, and parameters most commonly used to assess leak in this population. The multiple variables proposed in structured patient scenarios can be used to derive a definition for capillary leak.

Conflict of Interest

Dr. Faustino's institution received funding from the American Heart Association. The remaining authors have disclosed that they do not have any potential conflict of interest.

Acknowledgments

This work is funded by NICHD: T32HD068201. The authors would like to thank the PALISI Network for assistance in survey development and distribution.

References

- Pober JS, Sessa WC. Inflammation and the blood microvascular system. *Cold Spring Harb Perspect Biol* 2015;7(1):a016345
- Wetzel RC. The intensivist's system. *Crit Care Med* 1993;21(9, Suppl):S341–S344
- Deanfield JE, Halcox JP, Rabelink TJ. Endothelial function and dysfunction: testing and clinical relevance. *Circulation* 2007; 115(10):1285–1295
- Fishel RS, Are C, Barbul A. Vessel injury and capillary leak. *Crit Care Med* 2003;31(8, Suppl):S502–S511
- Mehta D, Malik AB. Signaling mechanisms regulating endothelial permeability. *Physiol Rev* 2006;86(1):279–367
- Aird WC. Phenotypic heterogeneity of the endothelium: I. Structure, function, and mechanisms. *Circ Res* 2007;100(2):158–173
- Mano G, Gilmore V, Leventhal M. On the mechanism of vascular leakage caused by histamine type mediators. A microscopic study in vivo. *Circ Res* 1967;21(6):833–847
- McDonald DM, Thurston G, Baluk P. Endothelial gaps as sites for plasma leakage in inflammation. *Microcirculation* 1999;6(1): 7–22
- Pober JS, Sessa WC. Evolving functions of endothelial cells in inflammation. *Nat Rev Immunol* 2007;7(10):803–815
- Aird WC. The role of the endothelium in severe sepsis and multiple organ dysfunction syndrome. *Blood* 2003;101(10):3765–3777
- Cordemans C, De Laet I, Van Regenmortel N, et al. Fluid management in critically ill patients: the role of extravascular lung water, abdominal hypertension, capillary leak, and fluid balance. *Ann Intensive Care* 2012;2(Suppl 1):S1
- Katzenelson R, Perel A, Berkenstadt H, et al. Accuracy of transpulmonary thermodilution versus gravimetric measurement of extravascular lung water. *Crit Care Med* 2004;32(7):1550–1554
- Margarson MP, Soni NC. Plasma volume measurement in septic patients using an albumin dilution technique: comparison with the standard radio-labelled albumin method. *Intensive Care Med* 2005;31(2):289–295
- Morisawa K, Fujitani S, Taira Y, et al; PiCCO Pulmonary Edema Study Group. Difference in pulmonary permeability between indirect and direct acute respiratory distress syndrome assessed by the transpulmonary thermodilution technique: a prospective, observational, multi-institutional study. *J Intensive Care* 2014; 2(1):24

- 15 Esposito C, Gerlach H, Brett J, Stern D, Vlassara H. Endothelial receptor-mediated binding of glucose-modified albumin is associated with increased monolayer permeability and modulation of cell surface coagulant properties. *J Exp Med* 1989;170(4): 1387–1407
- 16 Demircan M, Gurunluoglu K, Karaman A, Mizrak B. Damaging Effects of Total Parenteral Nutrition Formula on Vascular Endothelium. *J Pediatr Gastroenterol Nutr* 2015;61(4): 464–468
- 17 Harvey KA, Xu Z, Pavlina TM, Zaloga GP, Siddiqui RA. Modulation of endothelial cell integrity and inflammatory activation by commercial lipid emulsions. *Lipids Health Dis* 2015;14:9
- 18 Petri M, Orbai AM, Alarcón GS, et al. Derivation and validation of the Systemic Lupus International Collaborating Clinics classification criteria for systemic lupus erythematosus. *Arthritis Rheum* 2012;64(8):2677–2686
- 19 Fries JF. Methodology of validation of criteria for SLE. *Scand J Rheumatol Suppl* 1987;65:25–30
- 20 Morrison W, Womer J, Nathanson P, et al. Pediatricians' Experience with Clinical Ethics Consultation: A National Survey. *J Pediatr* 2015;167(4):919–924.e1
- 21 Alfares FA, Jones MB, Ramakrishnan K, Endicott KM, Zurakowski D, Shankar V, Nath DS. Perceptions of Bedside Cardiac Critical Care Registered Nurses on 24 Hour Attending Intensivist Coverage. *Congenit Heart Dis* 2016;11(4):354–358
- 22 Radabaugh CL, Ruch-Ross HS, Riley CL, et al. Practice Patterns in Pediatric Critical Care Medicine: Results of a Workforce Survey. *Pediatr Crit Care Med* 2015;16(8):e308–e312